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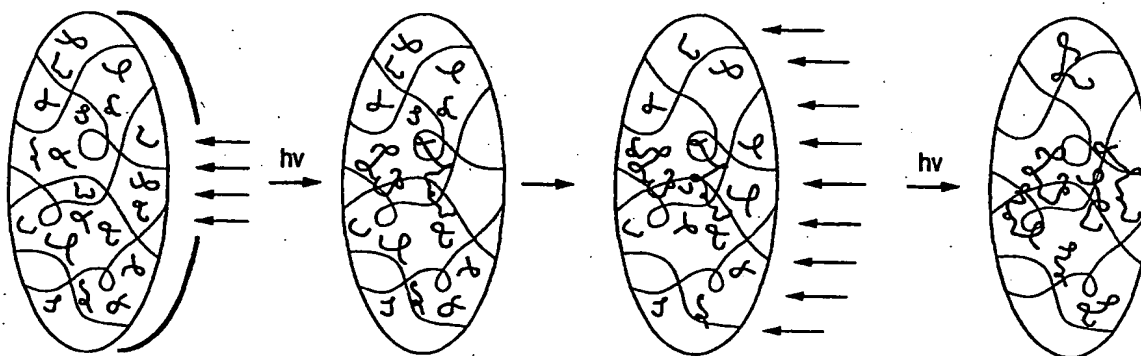
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(54) Title: LENSES CAPABLE OF POST-FABRICATION POWER MODIFICATION



(57) Abstract

The present invention relates to lenses that are capable of post-fabrication power modifications. In general, the inventive lenses comprise (i) a first polymer matrix and (ii) a refraction modulating composition that is capable of stimulus-induced polymerization dispersed therein. When at least a portion of the lens is exposed to an appropriate stimulus, the refraction modulating composition forms a second polymer matrix. The amount and location of the second polymer matrix may modify a lens characteristic such as lens power by changing its refractive index and/or by altering its shape. The inventive lenses have a number of applications in the electronics and medical fields as data storage means and as medical lenses, particularly intraocular lenses, respectively.

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LENSES CAPABLE OF POST-FABRICATION POWER MODIFICATION

BACKGROUND

Approximately two million cataract surgery procedures are performed in the United States annually. The procedure generally involves making an incision in the anterior lens capsule to remove the cataractous crystalline lens and implanting an intraocular lens in its place. The power of the implanted lens is selected (based upon pre-operative measurements of ocular length and corneal curvature) to enable the patient to see without additional corrective measures (*e.g.*, glasses or contact lenses). Unfortunately, due to errors in measurement, and/or variable lens positioning and wound healing, about half of all patients undergoing this procedure will not enjoy optimal vision without correction after surgery. Brandser *et al.*, *Acta Ophthalmol Scand* 75:162-165 (1997); Oshika *et al.*, *J cataract Refract Surg* 24:509-514 (1998). Because the power of prior art intraocular lenses generally cannot be adjusted once they have been implanted, the patient typically must choose between replacing the implanted lens with another lens of a different power or be resigned to the use of additional corrective lenses such as glasses or contact lenses. Since the benefits typically do not outweigh the risks of the former, it is almost never done.

An intraocular lens whose power may be adjusted after implantation and subsequent wound healing would be an ideal solution to post-operative refractive errors associated with cataract surgery. Moreover, such a lens would have wider applications and may be used to correct more typical conditions such as myopia, hyperopia, and astigmatism. Although surgical procedures such as LASIK which uses a laser to reshape the cornea are available, only low to moderate myopia and hyperopia may be readily treated. In contrast, an intraocular lens, which would function just like glasses or contact lenses to correct for the refractive error of the natural eye, could be implanted in the eye of any patient. Because the power of the implanted lens may be adjusted, post-operative refractive errors due to measurement irregularities and/or variable lens positioning and wound healing may be fine tuned *in-situ*.

SUMMARY

The present invention relates to optical elements, particularly medical lenses and methods of using the same. In general, the inventive lens comprises (i) a first polymer matrix and
5 (ii) a refraction modulating composition that is capable of stimulus-induced polymerization dispersed therein. In one embodiment, when at least a portion of the lens is exposed to an appropriate stimulus, the refraction modulating composition forms a second polymer matrix, the formation of which modifies lens power.

10

BRIEF DESCRIPTIONS OF THE DRAWINGS

Figure 1 is a schematic of a lens of the present invention being irradiated in the center followed by irradiation of the entire lens to "lock in" the modified lens power.

15 Figure 2 illustrates the prism irradiation procedure that is used to quantify the refractive index changes after being exposed to various amounts of irradiation.

Figure 3 shows unfiltered moiré fringe patterns of an inventive IOL. The angle between the two Ronchi rulings was set at 12° and the displacement distance between the first and
20 second moiré patterns was 4.92 mm.

Figure 4 is a Ronchigram of an inventive IOL. The Ronchi pattern corresponds to a 2.6 mm central region of the lens.

25 Figure 5 is a schematic illustrating a second mechanism whereby the formation of the second polymer matrix modulates a lens property by altering lens shape.

Figure 6 are Ronchi interferograms of an IOL before and after laser treatment depicting approximately a +8.6 diopter change in lens power within the eye. The spacing of
30 alternative light and dark bands is proportional to lens power.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention relates to optical elements (*e.g.*, lenses and prisms) that are capable of post-fabrication power modifications. More particularly, the present invention relates to intraocular lenses whose power may be adjusted *in-situ* after implantation in the eye.

5

The inventive optical elements comprise a first polymer matrix and a refraction modulating composition dispersed therein. The first polymer matrix forms the optical element framework and is generally responsible for many of its material properties. The refraction modulating composition ("RMC") may be a single compound or a combination
10 of compounds that is capable of stimulus-induced polymerization, preferably photopolymerization. As used herein, the term "polymerization" refers to a reaction wherein at least one of the components of the refraction modulating composition reacts to form at least one covalent or physical bond with either a like component or with a different component. The identities of the first polymer matrix and the refraction modulating
15 compositions will depend on the end use of the optical element. However, as a general rule, the first polymer matrix and the refraction modulating composition are selected such that the components that comprise the refraction modulating composition are capable of diffusion within the first polymer matrix. Put another way, a loose first polymer matrix will tend to be paired with larger RMC components and a tight first polymer matrix will
20 tend to be paired with smaller RMC components.

Upon exposure to an appropriate energy source (*e.g.*, heat or light), the refraction modulating composition typically forms a second polymer matrix in the exposed region of the optical element. The presence of the second polymer matrix changes the material
25 characteristics of this portion of the optical element to modulate its refraction capabilities. In general, the formation of the second polymer matrix typically increases the refractive index of the affected portion of the optical element. After exposure, the refraction modulating composition in the unexposed region will migrate into the exposed region over time. The amount of RMC migration into the exposed region is time dependent and
30 may be precisely controlled. If enough time is permitted, the RMC components will re-equilibrate and redistribute throughout optical element (*i.e.*, the first polymer matrix, including the exposed region). When the region is re-exposed to the energy source, the

refraction modulating composition ("RMC") that has since migrated into the region (which may be less than if the RMC composition were allowed to re-equilibrate) polymerizes to further increase the formation of the second polymer matrix. This process (exposure followed by an appropriate time interval to allow for diffusion) may be repeated until the exposed region of the optical element has reached the desired property (e.g., power, refractive index, or shape). At this point, the entire optical element is exposed to the energy source to "lock-in" the desired lens property by polymerizing the remaining RMC components that are outside the exposed region before the components can migrate into the exposed region. In other words, because freely diffusable RMC components are no longer available, subsequent exposure of the optical element to an energy source cannot further change its power. Figure 1 illustrates one inventive embodiment, refractive index modulation (thus lens power modulation) followed by a lock in.

The first polymer matrix is a covalently or physically linked structure that functions as an optical element and is formed from a first polymer matrix composition ("FPMC"). In general, the first polymer matrix composition comprises one or more monomers that upon polymerization will form the first polymer matrix. The first polymer matrix composition optionally may include any number of formulation auxiliaries that modulate the polymerization reaction or improve any property of the optical element. Illustrative examples of suitable FPMC monomers include acrylics, methacrylates, phosphazenes, siloxanes, vinyls, homopolymers and copolymers thereof. As used herein, a "monomer" refers to any unit (which may itself either be a homopolymer or copolymer) which may be linked together to form a polymer containing repeating units of the same. If the FPMC monomer is a copolymer, it may be comprised of the same type of monomers (e.g., two different siloxanes) or it may be comprised of different types of monomers (e.g., a siloxane and an acrylic).

In one embodiment, the one or more monomers that form the first polymer matrix are polymerized and cross-linked in the presence of the refraction modulating composition. In another embodiment, polymeric starting material that forms the first polymer matrix is cross-linked in the presence of the refraction modulating composition. Under either

scenario, the RMC components must be compatible with and not appreciably interfere with the formation of the first polymer matrix. Similarly, the formation of the second polymer matrix should also be compatible with the existing first polymer matrix. Put another way, the first polymer matrix and the second polymer matrix should not phase
5 separate and light transmission by the optical element should be unaffected.

As described previously, the refraction modulating composition may be a single component or multiple components so long as: (i) it is compatible with the formation of the first polymer matrix; (ii) it remains capable of stimulus-induced polymerization after
10 the formation of the first polymer matrix; and (iii) it is freely diffusible within the first polymer matrix. In preferred embodiments, the stimulus-induced polymerization is photo-induced polymerization.

The inventive optical elements have numerous applications in the electronics and data
15 storage industries. Another application for the present invention is as medical lenses, particularly as intraocular lenses.

In general, there are two types of intraocular lenses ("IOLs"). The first type of an intraocular lens replaces the eye's natural lens. The most common reason for such a
20 procedure is cataracts. The second type of intraocular lens supplements the existing lens and functions as a permanent corrective lens. This type of lens (sometimes referred to as a phakic intraocular lens) is implanted in the anterior or posterior chamber to correct any refractive errors of the eye. In theory, the power for either type of intraocular lenses required for emmetropia (*i.e.*, perfect focus on the retina from light at infinity) can be
25 precisely calculated. However, in practice, due to errors in measurement of corneal curvature, and/or variable lens positioning and wound healing, it is estimated that only about half of all patients undergoing IOL implantation will enjoy the best possible vision without the need for additional correction after surgery. Because prior art IOLs are generally incapable of post-surgical power modification, the remaining patients must
30 resort to other types of vision correction such as external lenses (*e.g.*, glasses or contact lenses) or cornea surgery. The need for these types of additional corrective measures is obviated with the use of the intraocular lenses of the present invention.

The inventive intraocular lens comprises a first polymer matrix and a refraction modulating composition dispersed therein. The first polymer matrix and the refraction modulating composition are as described above with the additional requirement that the
5 resulting lens be biocompatible.

Illustrative examples of a suitable first polymer matrix include: poly-acrylates such as poly-alkyl acrylates and poly-hydroxyalkyl acrylates; poly-methacrylates such as poly-methyl methacrylate ("PMMA"), poly-hydroxyethyl methacrylate ("PHEMA"), and poly-
10 hydroxypropyl methacrylate ("HPMA"); poly-vinyls such as poly-styrene and poly-vinylpyrrolidone ("PNVP"); poly-siloxanes such as poly-dimethylsiloxane; poly-phosphazenes, and copolymers of thereof. U.S. Patent No. 4,260,725 and patents and references cited therein (which are all incorporated herein by reference) provide more specific examples of suitable polymers that may be used to form the first polymer matrix.

15

In preferred embodiments, the first polymer matrix generally possesses a relatively low glass transition temperature (" T_g ") such that the resulting IOL tends to exhibit fluid-like and/or elastomeric behavior, and is typically formed by crosslinking one or more polymeric starting materials wherein each polymeric starting material includes at least
20 one crosslinkable group. Illustrative examples of suitable crosslinkable groups include but are not limited to hydride, acetoxo, alkoxy, amino, anhydride, aryloxy, carboxy, enoxy, epoxy, halide, isocyno, olefinic, and oxime. In more preferred embodiments, each polymeric starting material includes terminal monomers (also referred to as endcaps) that are either the same or different from the one or more monomers that comprise the
25 polymeric starting material but include at least one crosslinkable group. In other words, the terminal monomers begin and end the polymeric starting material and include at least one crosslinkable group as part of its structure. Although it is not necessary for the practice of the present invention, the mechanism for crosslinking the polymeric starting material preferably is different than the mechanism for the stimulus-induced
30 polymerization of the components that comprise the refraction modulating composition. For example, if the refraction modulating composition is polymerized by photo-induced polymerization, then it is preferred that the polymeric starting materials have

crosslinkable groups that are polymerized by any mechanism other than photo-induced polymerization.

5 An especially preferred class of polymeric starting materials for the formation of the first polymer matrix is poly-siloxanes (also known as "silicones") endcapped with a terminal monomer which includes a crosslinkable group selected from the group consisting of acetoxymethyl, amino, alkoxy, halide, hydroxy, and mercapto. Because silicone IOLs tend to be flexible and foldable, generally smaller incisions may be used during the IOL implantation procedure. An example of an especially preferred polymeric starting material is bis(diacetoxymethylsilyl)-polydimethylsiloxane (which is poly-
10 dimethylsiloxane that is endcapped with a diacetoxymethylsilyl terminal monomer).

The refraction modulating composition that is used in fabricating IOLs is as described above except that it has the additional requirement of biocompatibility.

15 The refraction modulating composition is capable of stimulus-induced polymerization and may be a single component or multiple components so long as: (i) it is compatible with the formation of the first polymer matrix; (ii) it remains capable of stimulus-induced polymerization after the formation of the first polymer matrix; and (iii) it is freely diffusible within the first polymer matrix. In general, the same type of monomers that is
20 used to form the first polymer matrix may be used as a component of the refraction modulating composition. However, because of the requirement that the RMC monomers must be diffusible within the first polymer matrix, the RMC monomers generally tend to be smaller (*i.e.*, have lower molecular weights) than the monomers which form the first polymer matrix. In addition to the one or more monomers, the refraction modulating
25 composition may include other components such as initiators and sensitizers that facilitate the formation of the second polymer matrix.

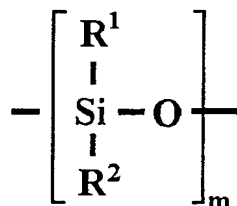
In preferred embodiments, the stimulus-induced polymerization is photo-polymerization. In other words, the one or more monomers that comprise the refraction modulating
30 composition each preferably includes at least one group that is capable of photopolymerization. Illustrative examples of such photopolymerizable groups include but are not limited to acrylate, allyloxy, cinnamoyl, methacrylate, stibenyl, and vinyl. In

more preferred embodiments, the refraction modulating composition includes a photoinitiator (any compound used to generate free radicals) either alone or in the presence of a sensitizer. Examples of suitable photoinitiators include acetophenones (e.g., -substituted haloacetophenones, and diethoxyacetophenone); 2,4-dichloromethyl-
 5 1,3,5-triazines; benzoin methyl ether; and o-benzoyl oximino ketone. Examples of suitable sensitizers include p-(dialkylamino)aryl aldehyde; N-alkylindolylidene; and bis[p-(dialkylamino)benzylidene] ketone.

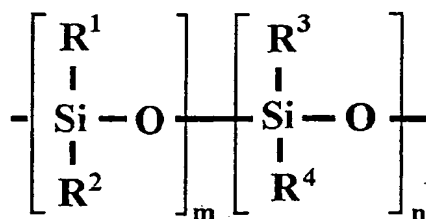
Because of the preference for flexible and foldable IOLs, an especially preferred class of
 10 RMC monomers is poly-siloxanes endcapped with a terminal siloxane moiety that includes a photopolymerizable group. An illustrative representation of such a monomer is



wherein Y is a siloxane which may be a monomer, a homopolymer or a copolymer
 15 formed from any number of siloxane units, and X and X¹ may be the same or different and are each independently a terminal siloxane moiety that includes a photopolymerizable group. An illustrative example of Y include



and



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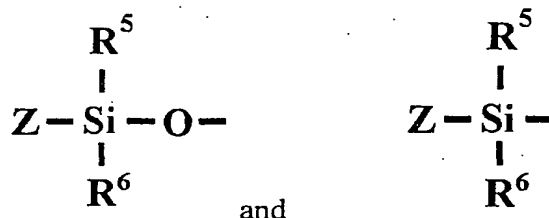
wherein: m and n are independently each an integer and

R¹, R², R³, and R⁴ are independently each hydrogen, alkyl (primary, secondary, tertiary, cyclo), aryl, or heteroaryl. In preferred embodiments, R¹, R², R³, and R⁴ is a C₁-C₁₀ alkyl or phenyl. Because RMC monomers with a relatively high aryl

content have been found to produce larger changes in the refractive index of the inventive lens, it is generally preferred that at least one of R^1 , R^2 , R^3 , and R^4 is an aryl, particularly phenyl. In more preferred embodiments, R^1 , R^2 , and R^3 are the same and are methyl, ethyl or propyl and R^4 is phenyl.

5

Illustrative examples of X and X^1 (or X^1 and X depending on how the RMC polymer is depicted) are

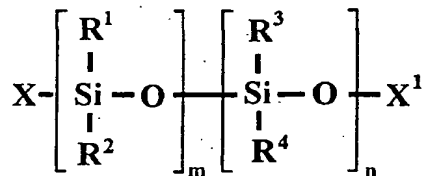


respectively wherein:

- 10 R^5 and R^6 are independently each hydrogen, alkyl, aryl, or heteroaryl; and
Z is a photopolymerizable group.

- In preferred embodiments, R^5 and R^6 are independently each a C_1 - C_{10} alkyl or phenyl and Z is a photopolymerizable group that includes a moiety selected from the group
15 consisting of acrylate, allyloxy, cinnamoyl, methacrylate, stibenyl, and vinyl. In more preferred embodiments, R^5 and R^6 is methyl, ethyl, or propyl and Z is a photopolymerizable group that includes an acrylate or methacrylate moiety.

In especially preferred embodiments, an RMC monomer is of the following formula

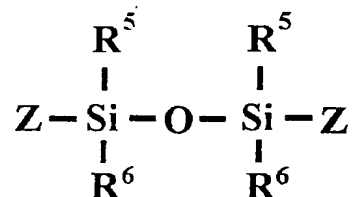


20

wherein X and X^1 are the same and R^1 , R^2 , R^3 , and R^4 are as defined previously.

- Illustrative examples of such RMC monomers include dimethylsiloxane-diphenylsiloxane copolymer endcapped with a vinyl dimethylsilane group; dimethylsiloxane-methylphenylsiloxane copolymer endcapped with a methacryloxypropyl dimethylsilane
25 group; and dimethylsiloxane endcapped with a methacryloxypropyldimethylsilane group.

Although any suitable method may be used, a ring-opening reaction of one or more cyclic siloxanes in the presence of triflic acid has been found to be a particularly efficient method of making one class of inventive RMC monomers. Briefly, the method comprises
 5 contacting a cyclic siloxane with a compound of the formula



in the presence of triflic acid wherein R^5 , R^6 , and Z are as defined previously. The cyclic siloxane may be a cyclic siloxane monomer, homopolymer, or copolymer. Alternatively, more than one cyclic siloxane may be used. For example, a cyclic dimethylsiloxane
 10 tetramer and a cyclic methyl-phenylsiloxane trimer are contacted with bis-methacryloxypropyltetramethyldisiloxane in the presence of triflic acid to form a dimethyl-siloxane methyl-phenylsiloxane copolymer that is endcapped with a methacryloxypropyl-dimethylsilane group, an especially preferred RMC monomer.

15 The inventive IOLs may be fabricated with any suitable method that results in a first polymer matrix with one or more components which comprise the refraction modulating composition dispersed therein, and wherein the refraction modulating composition is capable of stimulus-induced polymerization to form a second polymer matrix. In general, the method for making an inventive IOL is the same as that for making an inventive
 20 optical element. In one embodiment, the method comprises

mixing a first polymer matrix composition with a refraction modulating composition to form a reaction mixture;

placing the reaction mixture into a mold;

polymerizing the first polymer matrix composition to form said optical element;

25 and,

removing the optical element from the mold.

The type of mold that is used will depend on the optical element being made. For example, if the optical element is a prism, then a mold in the shape of a prism is used. Similarly, if the optical element is an intraocular lens, then an intraocular lens mold is

used and so forth. As described previously, the first polymer matrix composition comprises one or more monomers for forming the first polymer matrix and optionally includes any number of formulation auxiliaries that either modulate the polymerization reaction or improve any property (whether or not related to the optical characteristic) of the optical element. Similarly, the refraction modulating composition comprises one or more components that together are capable of stimulus-induced polymerization to form the second polymer matrix. Because flexible and foldable intraocular lenses generally permit smaller incisions, it is preferred that both the first polymer matrix composition and the refraction modulating composition include one or more silicone-based or low T_g acrylic monomers when the inventive method is used to make IOLs.

A key advantage of the intraocular lens of the present invention is that an IOL property may be modified after implantation within the eye. For example, any errors in the power calculation due to imperfect corneal measurements and/or variable lens positioning and wound healing may be modified in a post surgical outpatient procedure.

In addition to the change in the IOL refractive index, the stimulus-induced formation of the second polymer matrix has been found to affect the IOL power by altering the lens curvature in a predictable manner. As a result, both mechanisms may be exploited to modulate an IOL property, such as power, after it has been implanted within the eye. In general, the method for implementing an inventive IOL having a first polymer matrix and a refraction modulating composition dispersed therein, comprises:

- (a) exposing at least a portion of the lens to a stimulus whereby the stimulus induces the polymerization of the refraction modulating composition.
- If after implantation and wound healing, no IOL property needs to be modified, then the exposed portion is the entire lens. The exposure of the entire lens will lock in the then-existing properties of the implanted lens.

However, if a lens characteristic such as its power needs to be modified, then only a portion of the lens (something less than the entire lens) would be exposed. In one embodiment, the method of implementing the inventive IOL further comprises:

- (b) waiting an interval of time; and

(c) re-exposing the portion of the lens to the stimulus.

This procedure generally will induce the further polymerization of the refraction modulating composition within the exposed lens portion. Steps (b) and (c) may be repeated any number of times until the intraocular lens (or optical element) has reached
5 the desired lens characteristic. At this point, the method may further include the step of exposing the entire lens to the stimulus to lock-in the desired lens property.

In another embodiment wherein a lens property needs to be modified, a method for implementing an inventive IOL comprises:

- 10 (a) exposing a first portion of the lens to a stimulus whereby the stimulus induces the polymerization of the refraction modulating composition; and
(b) exposing a second portion of the lens to the stimulus.

The first lens portion and the second lens portion represent different regions of the lens although they may overlap. Optionally, the method may include an interval of time
15 between the exposures of the first lens portion and the second lens portion. In addition, the method may further comprise re-exposing the first lens portion and/or the second lens portion any number of times (with or without an interval of time between exposures) or may further comprise exposing additional portions of the lens (*e.g.*, a third lens portion, a fourth lens portion, etc.). Once the desired property has been reached, then the method
20 may further include the step of exposing the entire lens to the stimulus to lock-in the desired lens property.

In general, the location of the one or more exposed portions will vary depending on the type of refractive error being corrected. For example, in one embodiment, the exposed
25 portion of the IOL is the optical zone which is the center region of the lens (*e.g.*, between about 4 mm and about 5 mm in diameter). Alternatively, the one or more exposed lens portions may be along IOL's outer rim or along a particular meridian. In preferred embodiments, the stimulus is light. In more preferred embodiments, the light is from a laser source.

30 In summary, the present invention relates to a novel optical element that comprises (i) a first polymer matrix and (ii) a refraction modulating composition that is capable of

stimulus-induced polymerization dispersed therein. When at least a portion of the optical element is exposed to an appropriate stimulus, the refraction modulating composition forms a second polymer matrix. The amount and location of the second polymer matrix modifies a property such as the power of the optical element by changing its refractive index and/or by altering its shape.

EXAMPLE 1

Materials comprising various amounts of (a) poly-dimethylsiloxane endcapped with diacetoxymethylsilane ("PDMS") (36000 g/mol), (b) dimethylsiloxane-diphenylsiloxane copolymer endcapped with vinyl-dimethyl silane ("DMDPS") (15,500 g/mol), and (c) a UV-photoinitiator, 2,2-dimethoxy-2-phenylacetophenone ("DMPA") as shown by Table 1 were made and tested. PDMS is the monomer which forms first polymer matrix, and DMDPS and DMPA together comprise the refraction modulating composition.

TABLE 1

	PDMS (wt.%)	DMDPS (wt.%)	DMPA (wt.%) ^a
1	90	10	1.5
2	80	20	1.5
3	75	25	1.5
4	70	30	1.5

^a wt % with respect to DMDPS.

Briefly, appropriate amounts of PDMS (Gelest DMS-D33; 36000 g/mol), DMDPS (Gelest PDV-0325; 3.0-3.5 mole% diphenyl, 15,500 g/mol), and DMPA (Acros; 1.5 wt% with respect to DMDPS) were weighed together in an aluminum pan, manually mixed at room temperature until the DMPA dissolved, and degassed under pressure (5 mtorr) for 2-4 minutes to remove air bubbles. Photosensitive prisms were fabricated by pouring the resulting silicone composition into a mold made of three glass slides held together by scotch tape in the form of a prism and sealed at one end with silicone caulk. The prisms are ~5 cm long and the dimensions of the three sides are ~8 mm each. The

PDMS in the prisms was moisture cured and stored in the dark at room temperature for a period of 7 days to ensure that the resulting first polymer matrix was non-tacky, clear, and transparent.

- 5 The amount of photoinitiator (1.5 wt. %) was based on prior experiments with fixed RMC monomer content of 25% in which the photoinitiator content was varied. Maximal refractive index modulation was observed for compositions containing 1.5% and 2 wt. % photoinitiator while saturation in refractive index occurred at 5 wt. %.

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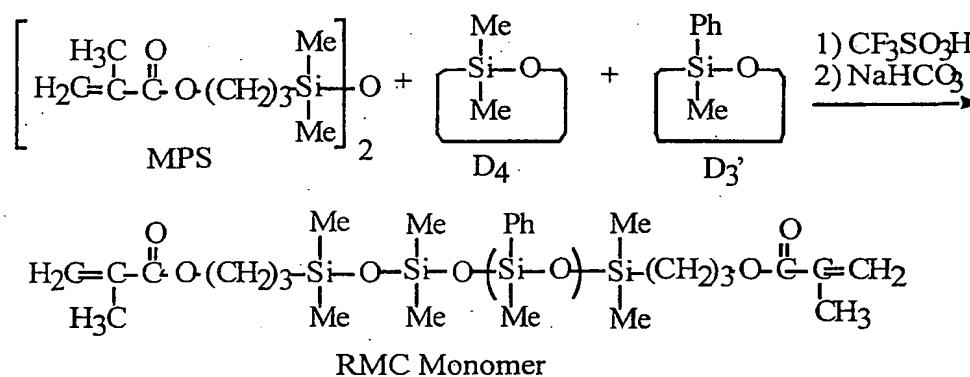
EXAMPLE 2

Synthesis RMC monomers

- As illustrated by Scheme 1, commercially available cyclic dimethylsiloxane tetramer ("D₄"), cyclic methylphenylsiloxane trimer ("D₃'") in various ratios were ring-opened by
 15 triflic acid and bis-methacryloxypropyltetramethyldisiloxane ("MPS") were reacted in a one pot synthesis. U.S. Patent No. 4,260,725; Kunzler, J. F., Trends in Polymer Science, 4: 52-59 (1996); Kunzler et al. J. Appl. Poly. Sci., 55: 611-619 (1995); and Lai et al., J. Poly. Sci. A. Poly. Chem., 33: 1773-1782 (1995).

20

SCHEME 1



- Briefly, appropriate amounts of MPS, D₄, and D₃' were stirred in a vial for 1.5-2 hours. An appropriate amount of triflic acid was added and the resulting mixture was stirred for another 20 hours at room temperature. The reaction mixture was diluted with hexane,
 25 neutralized (the acid) by the addition of sodium bicarbonate, and dried by the addition of

anhydrous sodium sulfate. After filtration and rotovaporation of hexane, the RMC monomer was purified by further filtration through an activated carbon column. The RMC monomer was dried at 5 mtorr of pressure between 70-80 °C for 12-18 hours.

5 The amounts of phenyl, methyl, and endgroup incorporation were calculated from ¹H-NMR spectra that were run in deuterated chloroform without internal standard tetramethylsilane ("TMS"). Illustrative examples of chemical shifts for some of the synthesized RMC monomers follows. A 1000 g/mole RMC monomer containing 5.58 mole% phenyl (made by reacting: 4.85 g (12.5 mmole) of MPS; 1.68 g (4.1 mmole) of D₃'; 5.98 g (20.2 mmole) of D₄; and 108 μl (1.21 mmole) of triflic acid: δ = 7.56-7.57 ppm (m, 2H) aromatic; δ = 7.32-7.33 ppm (m, 3H) aromatic, δ = 6.09 ppm (d, 2H) olefinic, δ = 5.53 ppm (d, 2H) olefinic, δ = 4.07-4.10 ppm (t, 4H) -O-CH₂CH₂CH₂-, δ = 1.93 ppm (s, 6H) methyl of methacrylate, δ = 1.65-1.71 ppm (m, 4H) -O-CH₂CH₂CH₂-, δ = 0.54-0.58 ppm (m, 4H) -O-CH₂CH₂CH₂-Si, δ = 0.29-0.30 ppm (d, 3H), CH₃-Si-Phenyl, δ = 0.04-0.08 ppm (s, 50 H) (CH₃)₂Si of the backbone.

A 2000 g/mole RMC monomer containing 5.26 mole% phenyl (made by reacting: 2.32 g (6.0 mmole) of MPS; 1.94 g (4.7 mmole) of D₃'; 7.74 g (26.1 mmole) of D₄; and 136 μl (1.54 mmole) of triflic acid: δ = 7.54-7.58 ppm (m, 4H) aromatic, δ = 7.32-7.34 ppm (m, 6H) aromatic, δ = 6.09 ppm (d, 2H) olefinic, δ = 5.53 ppm (d, 2H) olefinic, δ = 4.08-4.11 ppm (t, 4H) -O-CH₂CH₂CH₂-, δ = 1.94 ppm (s, 6H) methyl of methacrylate, δ = 1.67-1.71 ppm (m, 4H) -O-CH₂CH₂CH₂-, δ = 0.54-0.59 ppm (m, 4H) -O-CH₂CH₂CH₂-Si, δ = 0.29-0.31 ppm (m, 6H), CH₃-Si-Phenyl, δ = 0.04-0.09 ppm (s, 112H) (CH₃)₂Si of the backbone.

25 A 4000 g/mole RMC monomer containing 4.16 mole% phenyl (made by reacting: 1.06 g (2.74 mmole) of MPS; 1.67 g (4.1 mmole) of D₃'; 9.28 g (31.3 mmole) of D₄; and 157 μl (1.77 mmole) of triflic acid: δ = 7.57-7.60 ppm (m, 8H) aromatic, δ = 7.32-7.34 ppm (m, 12H) aromatic, δ = 6.10 ppm (d, 2H) olefinic, δ = 5.54 ppm (d, 2H) olefinic, δ = 4.08-4.12 ppm (t, 4H) -O-CH₂CH₂CH₂-, δ = 1.94 ppm (s, 6H) methyl of methacrylate, δ = 1.65-1.74 ppm (m, 4H) -O-CH₂CH₂CH₂-, δ = 0.55-0.59 ppm (m, 4H) -O-CH₂CH₂CH₂-Si,

$\delta = 0.31$ ppm (m, 11H), $\text{CH}_3\text{-Si-Phenyl}$. $\delta = 0.07\text{-}0.09$ ppm (s, 272 H) $(\text{CH}_3)_2\text{Si}$ of the backbone.

Similarly, to synthesize dimethylsiloxane polymer without any methylphenylsiloxane units and endcapped with methacryloxypropyl dimethylsilane, the ratio of D_4 to MPS was varied without incorporating D_3 .

Molecular weights were calculated by $^1\text{H-NMR}$ and by gel permeation chromatography ("GPC"). Absolute molecular weights were obtained by universal calibration method using polystyrene and poly(methyl methacrylate) standards. Table 2 shows the characterization of other RMC monomers synthesized by the triflic acid ring opening polymerization.

TABLE 2

	Mole % Phenyl	Mole % Methyl	Mole % Methacrylate	Mn (NMR)	Mn (GPC)	n_D
A	6.17	87.5	6.32	1001	946	1.44061
B	3.04	90.8	6.16	985	716	1.43188
C	5.26	92.1	2.62	1906	1880	-----
D	4.16	94.8	1.06	4054	4200	1.42427
E	0	94.17	5.83	987	1020	1.42272
F	0	98.88	1.12	3661	4300	1.40843

At 10-40 wt%, these RMC monomers of molecular weights 1000 to 4000 g/mol with 3-6.2 mole % phenyl content are completely miscible, biocompatible, and form optically clear prisms and lenses when incorporated in the silicone matrix. RMC monomers with high phenyl content (4-6 mole %) and low molecular weight (1000-4000 g/mol) resulted in increases in refractive index change of 2.5 times and increases in speeds of diffusion of 3.5 to 5.0 times compared to the RMC monomer used in Table 1 (dimethylsiloxane-diphenylsiloxane copolymer endcapped with vinyl dimethyl silane ("DMDPS") (3-3.5 mole % diphenyl content, 15500 g/mol). These RMC monomers were used to make optical elements comprising: (a) poly-dimethylsiloxane endcapped with diacetoxymethylsilane ("PDMS") (36000 g/mol), (b) dimethylsiloxane methylphenylsiloxane copolymer that is endcapped with a methacryloxypropyldimethylsilane group, and (c) 2,2-dimethoxy-2-phenylacetophenone

("DMPA"). Note that component (a) is the monomer that forms the first polymer matrix and components (b) and (c) comprise the refraction modulating composition.

EXAMPLE 3

5 Fabrication of intraocular lenses ("IOL")

An intraocular mold was designed according to well-accepted standards. *See e.g.*, U.S. Patent Nos. 5,762,836; 5,141,678; and 5,213,825. Briefly, the mold is built around two plano-concave surfaces possessing radii of curvatures of -6.46 mm and/or -12.92 mm, respectively. The resulting lenses are 6.35 mm in diameter and possess a thickness
10 ranging from 0.64 mm, 0.98 mm, or 1.32 mm depending upon the combination of concave lens surfaces used. Using two different radii of curvatures in their three possible combinations and assuming a nominal refractive index of 1.404 for the IOL composition, lenses with pre-irradiation powers of 10.51 D (62.09 D in air), 15.75 D (92.44 in air), and 20.95 D (121.46 D in air) were fabricated.

15

EXAMPLE 4

Stability of Compositions against Leaching

Three IOLs were fabricated with 30 and 10 wt % of RMC monomers B and D
20 incorporated in 60 wt% of the PDMS matrix. After moisture curing of PDMS to form the first polymer matrix, the presence of any free RMC monomer in the aqueous solution was analyzed as follows. Two out of three lenses were irradiated three times for a period of 2 minutes using 340 nm light, while the third was not irradiated at all. One of the irradiated lenses was then locked by exposing the entire lens matrix to radiation. All three lenses
25 were mechanically shaken for 3 days in 1.0 M NaCl solution. The NaCl solutions were then extracted by hexane and analyzed by ¹H-NMR. No peaks due to the RMC monomer were observed in the NMR spectrum. These results suggest that the RMC monomers did not leach out of the matrix into the aqueous phase in all three cases. Earlier studies on a vinyl endcapped silicone RMC monomer showed similar results even after being stored in
30 1.0 M NaCl solution for more than one year.

EXAMPLE 5

Toxicological Studies in Rabbit Eyes

Sterilized, unirradiated and irradiated silicone IOLs (fabricated as described in Example 3) of the present invention and a sterilized commercially available silicone IOL were
5 implanted in albino rabbit eyes. After clinically following the eyes for one week, the rabbits were sacrificed. The extracted eyes were enucleated, placed in formalin and studied histopathologically. There is no evidence of corneal toxicity, anterior segment inflammation, or other signs of lens toxicity.

10

EXAMPLE 6

Irradiation of Silicone Prisms

Because of the ease of measuring refractive index change (n) and percent net refractive index change ($\% n$) of prisms, the inventive formulations were molded into prisms for
15 irradiation and characterization. Prisms were fabricated by mixing and pouring (a) 90-60 wt% of high M_n PDMS, (b) 10-40 wt% of RMC monomers in Table 2, and (c) 0.75 wt% (with respect to the RMC monomers) of the photoinitiator DMPA into glass molds in the form of prisms 5 cm long and 8.0 mm on each side. The silicone composition in the prisms was moisture cured and stored in the dark at room temperature for a period of 7
20 days to ensure that the final matrix was non-tacky, clear and transparent.

Two of the long sides of each prism were covered by a black background while the third was covered by a photomask made of an aluminum plate with rectangular windows (2.5 mm x 10 mm). Each prism was exposed to a flux of 1.2 mW/cm^2 of a collimated 340 nm
25 light (peak absorption of the photoinitiator) from a 1000 W Xe:Hg arc lamp for various time periods. The ANSI guidelines indicate that the maximum permissible exposure ("MPE") at the retina using 340 nm light for a 10-30000 s exposure is 1000 mJ/cm^2 .
Criteria for Exposure of Eye and Skin. *American National Standard Z136.1*: 31-42 (1993). The single dose intensity 1.2 mW/cm^2 of 340 nm light for a period of 2 minutes
30 corresponds to 144 mJ/cm^2 which is well within the ANSI guidelines. In fact, even the overall intensity for three exposures (432 mJ/cm^2) is well within the ANSI guidelines. Figure 2 is an illustration of the prism irradiation procedure.

The prisms were subject to both (i) continuous irradiation - one-time exposure for a known time period, and (ii) "staccato" irradiation - three shorter exposures with long intervals between them. During continuous irradiation, the refractive index contrast is dependent on the crosslinking density and the mole % phenyl groups, while in the interrupted irradiation, RMC monomer diffusion and further crosslinking also play an important role. During staccato irradiation, the RMC monomer polymerization depends on the rate of propagation during each exposure and the extent of interdiffusion of free RMC monomer during the intervals between exposures. Typical values for the diffusion coefficient of oligomers (similar to the 1000 g/mole RMC monomers used in the practice of the present invention) in a silicone matrix are on the order of 10^{-6} to 10^{-7} cm²/s. In other words, the inventive RMC monomers require approximately 2.8 to 28 hours to diffuse 1 mm (roughly the half width of the irradiated bands). The distance of a typical optical zone in an IOL is about 4 to about 5 mm across. However, the distance of the optical zone may also be outside of this range. After the appropriate exposures, the prisms were irradiated without the photomask (thus exposing the entire matrix) for 6 minutes using a medium pressure mercury-arc lamp. This polymerized the remaining silicone RMC monomers and thus "locked" the refractive index of the prism in place. Notably, the combined total irradiation of the localized exposures and the "lock-in" exposure was still within ANSI guidelines.

EXAMPLE 7

Prism Dose Response Curves

Inventive prisms fabricated from RMC monomers described by Table 2 were masked and initially exposed for 0.5, 1, 2, 5, and 10 minutes using 1.2 mW/cm² of the 340 nm line from a 1000 W Xe:Hg arc lamp. The exposed regions of the prisms were marked, the mask detached and the refractive index changes measured. The refractive index modulation of the prisms was measured by observing the deflection of a sheet of laser light passed through the prism. The difference in deflection of the beam passing through the exposed and unexposed regions was used to quantify the refractive index change (n) and the percentage change in the refractive index (% n).

After three hours, the prisms were remasked with the windows overlapping with the previously exposed regions and irradiated for a second time for 0.5, 1, 2, and 5 minutes (total time thus equaled 1, 2, 4, and 10 minutes respectively). The masks were detached and the refractive index changes measured. After another three hours, the prisms were exposed a third time for 0.5, 1, and 2 minutes (total time thus equaled 1.5, 3, and 6 minutes) and the refractive index changes were measured. As expected, the % n increased with exposure time for each prism after each exposure resulting in prototypical dose response curves. Based upon these results, adequate RMC monomer diffusion appears to occur in about 3 hours for 1000 g/mole RMC monomer.

All of the RMC monomers (B-F) except for RMC monomer A resulted in optically clear and transparent prisms before and after their respective exposures. For example, the largest % n for RMC monomers B, C, and D at 40 wt% incorporation into 60 wt% FPMC were 0.52%, 0.63% and 0.30% respectively which corresponded to 6 minutes of total exposure (three exposures of 2 minutes each separated by 3 hour intervals for RMC monomer B and 3 days for RMC monomers C and D). However, although it produced the largest change in refractive index (0.95%), the prism fabricated from RMC monomer A (also at 40 wt% incorporation into 60 wt% FPMC and 6 minutes of total exposure - three exposures of 2 minutes each separated by 3 hour intervals) turned somewhat cloudy. Thus, if RMC monomer A were used to fabricate an IOL, then the RMC must include less than 40 wt% of RMC monomer A or the % n must be kept below the point where the optical clarity of the material is compromised.

A comparison between the continuous and staccato irradiation for RMC A and C in the prisms shows that lower % n values occurs in prisms exposed to continuous irradiation as compared to those observed using staccato irradiations. As indicated by these results, the time interval between exposures (which is related to the amount of RMC diffusion from the unexposed to exposed regions) may be exploited to precisely modulate the refractive index of any material made from the inventive polymer compositions.

Exposure of the entire, previously irradiated prisms to a medium pressure Hg arc lamp polymerized any remaining free RMC, effectively locking the refractive index contrast. Measurement of the refractive index change before and after photolocking indicated no further modulation in the refractive index.

5

EXAMPLE 8

Optical characterization of IOLs

Talbot interferometry and the Ronchi test were used to qualitatively and quantitatively measure any primary optical aberrations (primary spherical, coma, astigmatism, field curvature, and distortion) present in pre- and post-irradiated lenses as well as quantifying changes in power upon photopolymerization.

In Talbot interferometry, the test IOL is positioned between the two Ronchi rulings with the second grating placed outside the focus of the IOL and rotated at a known angle, α_2 , with respect to the first grating. Superposition of the autoimage of the first Ronchi ruling ($p_1 = 300$ lines/inch) onto the second grating ($p_2 = 150$ lines/inch) produces moiré fringes inclined at an angle, θ . A second moiré fringe pattern is constructed by axial displacement of the second Ronchi ruling along the optic axis a known distance, d , from the test lens. Displacement of the second grating allows the autoimage of the first Ronchi ruling to increase in magnification causing the observed moiré fringe pattern to rotate to a new angle, θ_2 . Knowledge of moiré pitch angles permits determination of the focal length of the lens (or inversely its power) through the expression:

$$f = \frac{p_1}{p_2} d \left(\frac{1}{\tan \alpha_2 \sin \theta + \cos \theta} - \frac{1}{\tan \alpha_1 \sin \theta + \cos \theta} \right)^{-1}$$

25

To illustrate the applicability of Talbot interferometry to this work, moiré fringe patterns of one of the inventive, pre-irradiated IOLs (60 wt% PDMS, 30 wt% RMC monomer B, 10 wt% RMC monomer D, and 0.75% DMPA relative to the two RMC monomers) measured in air is presented in Figure 3. Each of the moiré fringes was fitted with a least squares fitting algorithm specifically designed for the processing of moiré patterns. The angle between the two Ronchi rulings was set at 12° , the displacement between the

30

second Ronchi ruling between the first and second moiré fringe patterns was 4.92 mm, and the pitch angles of the moiré fringes, measured relative to an orthogonal coordinate system defined by the optic axis of the instrument and crossing the two Ronchi rulings at 90°, were $\alpha_1 = -33.2 \pm 0.30^\circ$ and $\alpha_2 = -52.7 \pm 0.40^\circ$. Substitution of these values into the above equation results in a focal length of 10.71 ± 0.50 mm (power = 93.77 ± 4.6 D).

Optical aberrations of the inventive IOLs (from either fabrication or from the stimulus-induced polymerization of the RMC components) were monitored using the "Ronchi Test" which involves removing the second Ronchi ruling from the Talbot interferometer and observing the magnified autoimage of the first Ronchi ruling after passage through the test IOL. The aberrations of the test lens manifest themselves by the geometric distortion of the fringe system (produced by the Ronchi ruling) when viewed in the image plane. A knowledge of the distorted image reveals the aberration of the lens. In general, the inventive fabricated lenses (both pre and post irradiation treatments) exhibited sharp, parallel, periodic spacing of the interference fringes indicating an absence of the majority of primary-order optical aberrations, high optical surface quality, homogeneity of n in the bulk, and constant lens power. Figure 4 is an illustrative example of a Ronchigram of an inventive, pre-irradiated IOL that was fabricated from 60 wt% PDMS, 30 wt% RMC monomer B, 10 wt% RMC monomer D, and 0.75% of DMPA relative to the 2 RMC monomers.

The use of a single Ronchi ruling may also be used to measure the degree of convergence of a refracted wavefront (*i.e.*, the power). In this measurement, the test IOL is placed in contact with the first Ronchi ruling, collimated light is brought incident upon the Ronchi ruling, and the lens and the magnified autoimage is projected onto an observation screen. Magnification of the autoimage enables measurement of the curvature of the refracted wavefront by measuring the spatial frequency of the projected fringe pattern. These statements are quantified by the following equation:

$$P_r = \frac{1000}{L} \left(1 + \frac{d_s}{d} \right)$$

wherein P_v is the power of the lens expressed in diopters, L is the distance from the lens to the observing plane, d_s is the magnified fringe spacing of the first Ronchi ruling, and d is the original grating spacing.

5

EXAMPLE 9

Power changes from photopolymerization of the inventive IOLs

An inventive IOL was fabricated as described by Example 3 comprising 60 wt % PDMS ($n_D=1.404$), 30 wt % of RMC monomer B ($n_D=1.4319$), 10 wt % of RMC monomer D ($n_D=1.4243$), and 0.75 wt % of the photoinitiator DMPA relative to the combined weight percents of the two RMC monomers. The IOL was fitted with a 1 mm diameter photomask and exposed to 1.2 mW/cm^2 of 340 nm collimated light from a 1000 W Xe:Hg arc lamp for two minutes. The irradiated lens was then placed in the dark for three hours to permit polymerization and RMC monomer diffusion. The IOL was photolocked by continuously exposing the entire for six minutes using the aforementioned light conditions. Measurement of the moiré pitch angles followed by substitution into equation 1 resulted in a power of $95.1 \pm 2.9 \text{ D}$ ($f=10.52 \pm 0.32 \text{ mm}$) and $104.1 \pm 3.6 \text{ D}$ ($f=9.61 \text{ mm} \pm 0.32 \text{ mm}$) for the unirradiated and irradiated zones, respectively.

The magnitude of the power increase was more than what was predicted from the prism experiments where a 0.6% increase in the refractive index was routinely achieved. If a similar increase in the refractive index was achieved in the IOL, then the expected change in the refractive index would be 1.4144 to 1.4229. Using the new refractive index (1.4229) in the calculation of the lens power (in air) and assuming the dimensions of the lens did not change upon photopolymerization, a lens power of 96.71 D ($f=10.34 \text{ mm}$) was calculated. Since this value is less than the observed power of $104.1 \pm 3.6 \text{ D}$, the additional increase in power must be from another mechanism.

Further study of the photopolymerized IOL showed that subsequent RMC monomer diffusion after the initial radiation exposure leads to changes in the radius of curvature of the lens. See e.g., Figure 5. The RMC monomer migration from the unirradiated zone into the radiated zone causes either or both of anterior and posterior surfaces of the lens to

swell thus changing the radius of curvature of the lens. It has been determined that a 7% decrease in the radius of curvature for both surfaces is sufficient to explain the observed increase in lens power.

- 5 The concomitant change in the radius of curvature was further studied. An identical IOL described above was fabricated. A Ronchi interferogram of the IOL is shown in Figure 6a (left interferogram). Using a Talbot interferometer, the focal length of the lens was experimentally determined to be 10.52 ± 0.30 mm ($95.1 \text{ D} \pm 2.8 \text{ D}$). The IOL was then fitted with a 1mm photomask and irradiated with 1.2 mW/cm^2 of 340 collimated light
- 10 from a 1000 W Xe:Hg arc lamp continuously for 2.5 minutes. Unlike the previous IOL, this lens was not "locked in" three hours after irradiation. Figure 6b (right interferogram) is the Ronchi interferogram of the lens taken six days after irradiation. The most obvious feature between the two interference patterns is the dramatic increase in the fringe spacing, which is indicative of an increase in the refractive power of the lens.
- 15
- Measurement of the fringe spacings indicates an increase of approximately +38 diopters in air ($f \approx 7.5$ mm). This corresponds to a change in the order of approximately +8.6 diopters in the eye. Since most post-operative corrections from cataract surgery are within 2 diopters, this experiment indicates that the use of the inventive IOLS will permit
- 20 a relatively large therapeutic window.

EXAMPLE 10

Photopolymerization studies of non-phenyl-containing IOLs

- 25 Inventive IOLs containing non-phenyl containing RMC monomers were fabricated to further study the swelling from the formation of the second polymer matrix. An illustrative example of such an IOL was fabricated from 60 wt% PDMS, 30 wt% RMC monomer E, 10 wt% RMC monomer F, and 0.75% DMPA relative to the two RMC monomers. The pre-irradiation focal length of the resulting IOL was 10.76 mm ($92.94 \pm$
- 30 2.21 D).

In this experiment, the light source was a 325 nm laser line from a He:Cd laser. A 1 mm diameter photomask was placed over the lens and exposed to a collimated flux of 0.75 mW/cm^2 at 325 nm for a period of two minutes. The lens was then placed in the dark for three hours. Experimental measurements indicated that the focal length of the IOL

5 changed from $10.76 \text{ mm} \pm 0.25 \text{ mm}$ ($92.94 \text{ D} \pm 2.21 \text{ D}$) to $8.07 \text{ mm} \pm 0.74 \text{ mm}$ ($123.92 \text{ D} \pm 10.59 \text{ D}$) or a dioptric change of $+ 30.98 \text{ D} \pm 10.82 \text{ D}$ in air. This corresponds to an approximate change of $+ 6.68 \text{ D}$ in the eye. The amount of irradiation required to induce these changes is only 0.09 J/cm^2 , a value well under the ANSI maximum permissible exposure ("MPE") level of 1.0 J/cm^2 .

10

EXAMPLE 11

Monitoring for potential IOL changes from ambient light

The optical power and quality of the inventive IOLs were monitored to show that handling and ambient light conditions do not produce any unwanted changes in lens

15 power. A 1 mm open diameter photomask was placed over the central region of an inventive IOL (containing 60 wt% PDMS, 30 wt% RMC monomer E, 10 wt% RMC monomer F, and 0.75 wt% DMPA relative to the two RMC monomers), exposed to continuous room light for a period of 96 hours, and the spatial frequency of the Ronchi patterns as well as the moiré fringe angles were monitored every 24 hours. Using the

20 method of moiré fringes, the focal length measured in the air of the lens immediately after removal from the lens mold is $10.87 \pm 0.23 \text{ mm}$ ($92.00 \text{ D} \pm 1.98 \text{ D}$) and after 96 hours of exposure to ambient room light is $10.74 \text{ mm} \pm 0.25 \text{ mm}$ ($93.11 \text{ D} \pm 2.22 \text{ D}$). Thus, within the experimental uncertainty of the measurement, it is shown that ambient light does not induce any unwanted change in power. A comparison of the resulting Ronchi patterns

25 showed no change in spatial frequency or quality of the interference pattern, confirming that exposure to room light does not affect the power or quality of the inventive IOLs.

EXAMPLE 12

Effect of the lock in procedure of an irradiated IOL

An inventive IOL whose power had been modulated by irradiation was tested to see if the lock-in procedure resulted in further modification of lens power. An IOL fabricated from

60 wt% PDMS, 30 wt% RMC monomer E, 10 wt% RMC monomer F, and 0.75% DMPA relative to the two RMC monomers was irradiated for two minutes with 0.75 mW/cm^2 of the 325 nm laser line from a He:Cd laser and was exposed for eight minutes to a medium pressure Hg arc lamp. Comparisons of the Talbot images before and after the lock in procedure showed that the lens power remained unchanged. The sharp contrast of the interference fringes indicated that the optical quality of the inventive lens also remained unaffected.

To determine if the lock-procedure was complete, the IOL was refitted with a 1 mm diameter photomask and exposed a second time to 0.75 mW/cm^2 of the 325 laser line for two minutes. As before, no observable change in fringe space or in optical quality of the lens was observed.

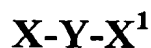
EXAMPLE 13

Monitoring for potential IOL changes from the lock-in

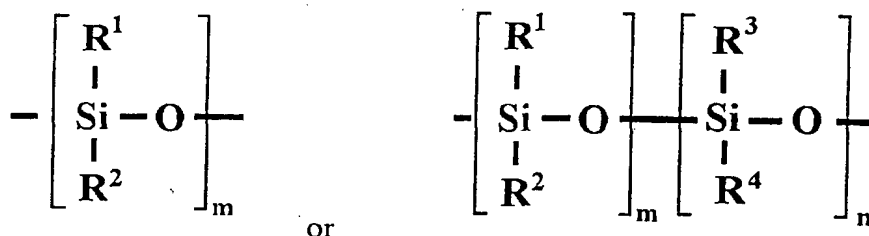
A situation may arise wherein the implanted IOL does not require post-operative power modification. In such cases, the IOL must be locked in so that its characteristic will not be subject to change. To determine if the lock-in procedure induces undesired changes in the refractive power of a previously unirradiated IOL, the inventive IOL (containing 60 wt% PDMS, 30 wt% RMC monomer E, 10 wt% RMC monomer F, and 0.75 wt% DMPA relative to the two RMC monomers) was subject to three 2 minute irradiations over its entire area that was separated by a 3 hour interval using 0.75 mW/cm^2 of the 325 laser line from a He:Cd laser. Ronchigrams and moiré fringe patterns were taken prior to and after each subsequent irradiation. The moiré fringe patterns taken of the inventive IOL in air immediately after removal from the lens mold and after the third 2 minute irradiation indicate a focal length of $10.50 \text{ mm} \pm 0.39 \text{ mm}$ ($95.24 \text{ D} \pm 3.69 \text{ D}$) and $10.12 \text{ mm} \pm 0.39 \text{ mm}$ ($93.28 \text{ D} \pm 3.53 \text{ D}$) respectively. These measurements indicate that photolocking a previously unexposed lens does not induce unwanted changes in power. In addition, no discernable change in fringe spacing or quality of the Ronchi fringes was detected indicating that the refractive power had not changed due to the lock-in.

What is claimed is:

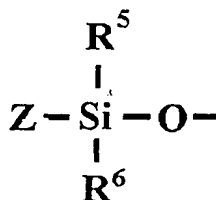
1. An optical element comprising:
a first polymer matrix and
a refraction modulating composition dispersed therein wherein the refraction modulating composition is capable of stimulus-induced polymerization.
2. The optical element as in claim 1 wherein the refraction modulating composition is capable of photo-induced polymerization.
3. The optical element as in claim 1 wherein the optical element is a prism.
4. The optical element as in claim 1 wherein the optical element is a lens.
5. A lens comprising:
a first polymer matrix and
a refraction modulating composition dispersed therein wherein the refraction modulating composition is capable of photo-induced polymerization.
6. The lens as in claim 5 wherein the first polymer matrix is selected from the group consisting of poly-acrylate, poly-methacrylate, poly-vinyl, poly-siloxane, and poly-phosphazene.
7. The lens as in claim 5 wherein the refraction modulating composition includes a component selected from the group consisting of an acrylate, methacrylate, vinyl, siloxane, and phosphazine.
8. The lens as in claim 5 wherein the refraction modulating composition comprises a monomer of the formula



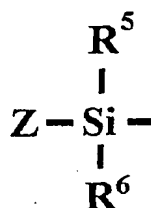
and a photoinitiator
wherein Y is



X is



and X¹ is



wherein: m and n are each independently an integer and
R¹, R², R³, R⁴, R⁵, and R⁶ are each independently selected from the group
consisting hydrogen, alkyl, aryl, and heteroaryl; and
Z is a photopolymerizable group.

9. The lens as in claim 6 wherein the first polymer matrix includes a poly-siloxane.
10. The lens as in claim 6 wherein the first polymer matrix includes a poly-acrylate.
11. The lens as in claim 8 wherein
R¹, R², R³, R⁴, R⁵, and R⁶ are each independently a C₁-C₁₀ alkyl or phenyl and
Z is includes a moiety selected from the group consisting of acrylate, allyloxy,
cinnamoyl, methacrylate, cinnamoyl, stibenyl, and vinyl.

12. The lens as in claim 11 wherein R^1 , R^2 , and R^3 , R^5 , and R^6 are selected from the group consisting of methyl, ethyl and propyl and R^4 is phenyl.
13. The lens as in claim 11 wherein
the monomer is (i) dimethylsiloxane-diphenylsiloxane copolymer endcapped with a vinyl dimethylsilane group, (ii) dimethylsiloxane-methylphenylsiloxane copolymer endcapped with a methacryloxypropyldimethylsilane group, or (iii) dimethylsiloxane encapped with a methacryloxypropyldimethylsilane group and
the photoinitiator is 2,2-dimethoxy-2-phenylacetophenone.
14. An intraocular lens comprising:
a polysiloxane matrix and a refraction modulating composition dispersed therein wherein the refraction modulating composition is capable of photo-induced polymerization.
15. The intraocular lens as in claim 14 wherein the polysiloxane matrix is polydimethyl siloxane endcapped with diacetoxymethylsilane.
16. The intraocular lens as in claim 14 wherein the refraction modulating composition comprises:
dimethylsiloxane-diphenylsiloxane copolymer endcapped with a vinyl dimethylsilane group; dimethylsiloxane-methylphenylsiloxane copolymer endcapped with a methacryloxypropyldimethylsilane group; or dimethylsiloxane encapped with a methacryloxypropyldimethylsilane group; and,
2,2-dimethoxy-2-phenylacetophenone.
17. A method of implementing an optical element having a refractive modulating composition dispersed therein, comprising:
(a) exposing at least a portion of the optical element to a stimulus whereby the stimulus induces the polymerization of the refraction modulating composition.
18. The method as in claim 17 wherein the optical element is a prism or a lens.

19. The method as in claim 17 wherein the exposed portion represents the entire optical element.
20. The method as in claim 17 further comprising
 - (b) waiting an interval of time; and
 - (c) re-exposing the portion of the optical element to the stimulus to induce the further polymerization of the refraction modulating composition within said portion.
21. The method as in claim 20 further comprising repeating steps (b) and (c).
22. The method as in claim 20 further comprising:
exposing the entire optical element to the stimulus.
23. A method of implementing an intraocular lens having a refractive modulating composition dispersed therein and implanted within the eye, comprising:
 - (a) exposing at least a portion of the lens to a light source whereby the light source induces the polymerization of the refraction modulating composition.
24. The method as in claim 23 wherein the exposed portion represents the entire intraocular lens.
25. The method as in claim 23 further comprising:
 - (b) waiting an interval of time; and
 - (c) re-exposing the portion of the lens to the light source to induce the further polymerization of the refraction modulating composition within said portion.
26. The method as in claim 23 further comprising repeating steps (b) and (c).
27. The method as in claim 23 further comprising:

exposing the entire lens to the light source.

28. The method as in claim 23 wherein the exposed portion is the optical zone of the lens.
29. The method as in claim 23 wherein the exposed portion is the outer rim of the lens.
30. The method as in claim 23 wherein the exposed portion is along a meridian of the lens.
31. A method of implementing an intraocular lens having a refractive modulating composition dispersed therein and implanted within the eye, comprising:
 - (a) exposing a first portion of the lens to a light source whereby the light source induces the polymerization of the refraction modulating composition and
 - (b) exposing a second portion of the lens to the light source.
32. The method as in claim 31 further comprising exposing a third portion of the lens to a light source.
33. The method as in claim 31 further comprising exposing the entire lens to the light source.
34. A method for fabricating an optical element, comprising:
 - mixing a first polymer matrix composition with a refraction modulating composition to form a reaction mixture;
 - placing the reaction mixture into a mold;
 - polymerizing the first polymer matrix composition to form a first polymer matrix with the refraction modulating composition dispersed therein; and,
 - removing said optical element from the mold.

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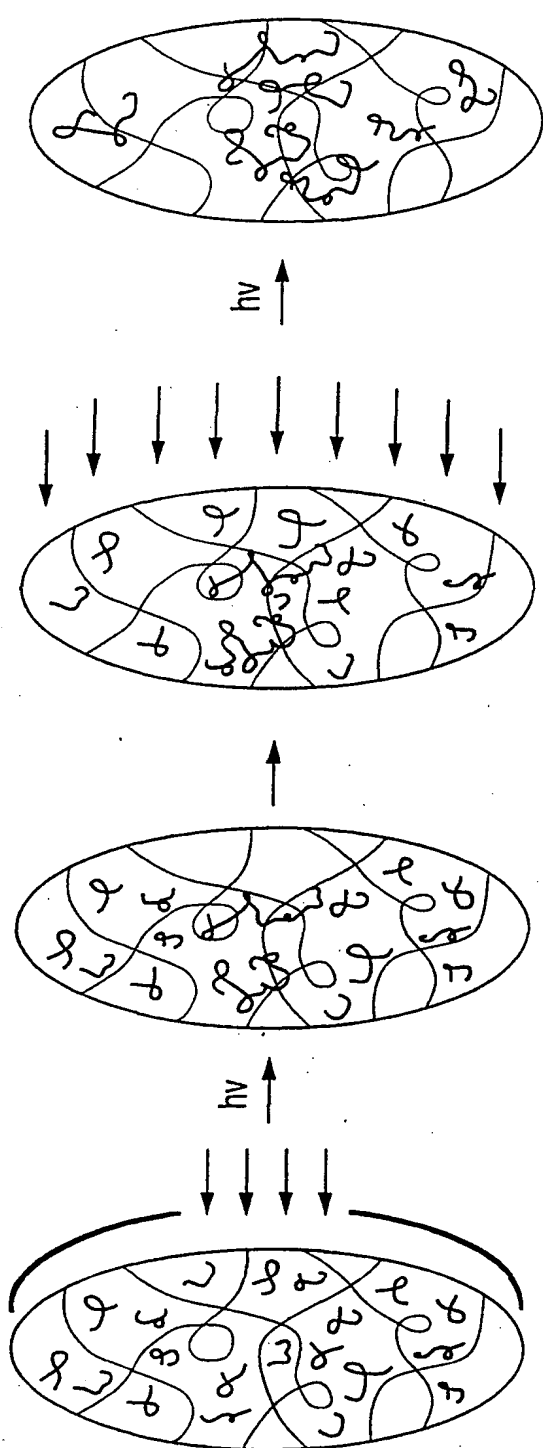


FIG. 1

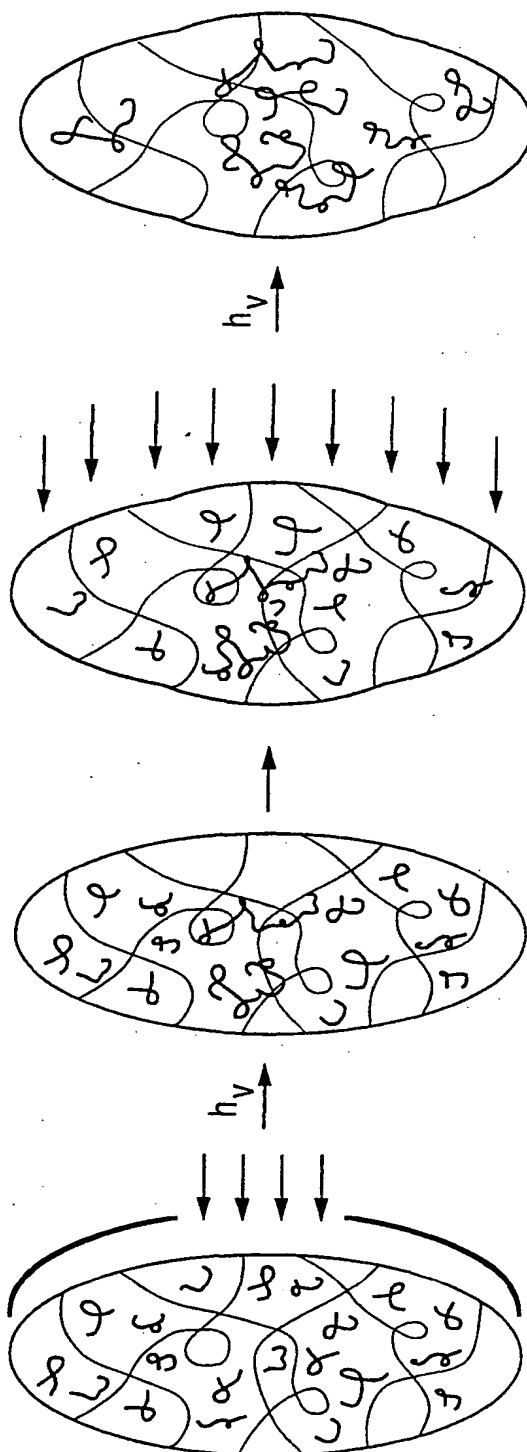


FIG. 5

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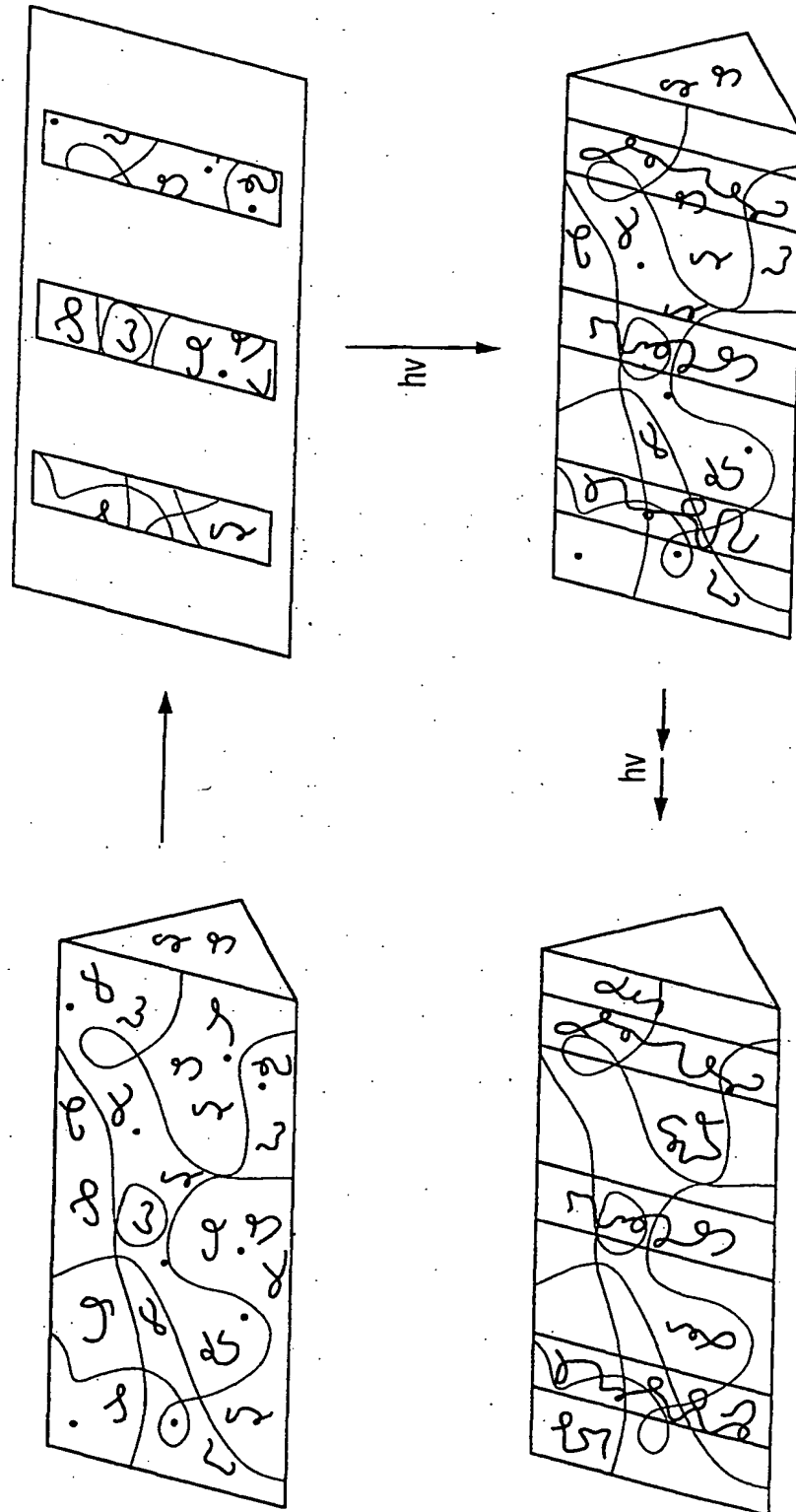


FIG. 2

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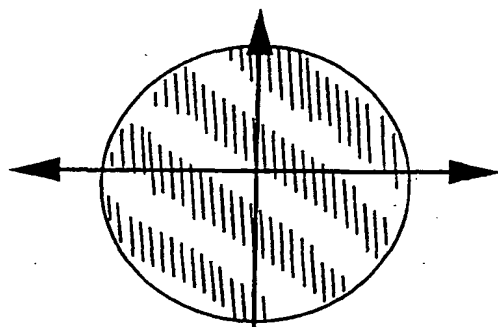


FIG. 3A

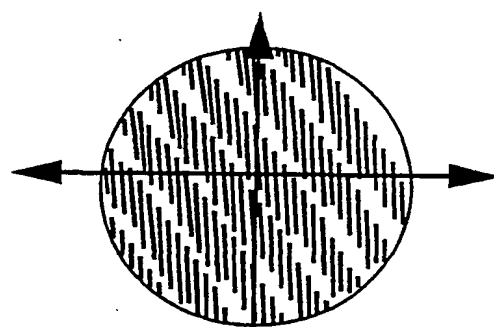


FIG. 3B

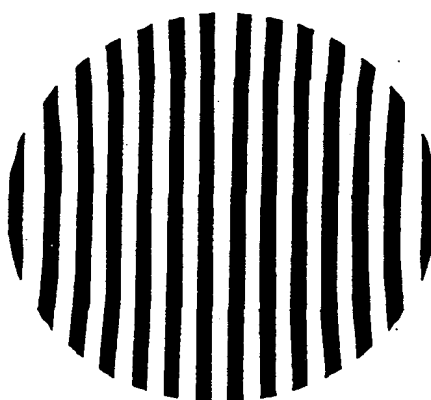


FIG. 4

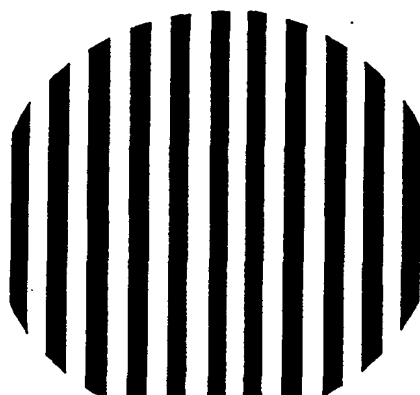


FIG. 6A



FIG. 6B

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/23728

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F2/16 G02B1/04

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61F G02B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X A	EP 0 689 067 A (FUJITSU LTD) 27 December 1995 (1995-12-27) page 3, line 6 - line 16 page 10, line 10 - line 28; figure 5AB	1,2,5,17 14,23,31
X A	PATENT ABSTRACTS OF JAPAN vol. 010, no. 180 (P-471), 24 June 1986 (1986-06-24) & JP 61 027501 A (NIPPON SHEET GLASS CO LTD; OTHERS: 01), 7 February 1986 (1986-02-07) abstract; figure	1,4, 17-19 5,34
	-/-	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search

12 May 2000

Date of mailing of the international search report

22/05/2000

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INTERNATIONAL SEARCH REPORT

Int'l. Serial Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 010, no. 022 (P-424), 28 January 1986 (1986-01-28) & JP 60 175009 A (NIHON ITA GLASS KK;OTHERS: 01), 9 September 1985 (1985-09-09)	1,4, 17-19
A	abstract; figure	5,34
X	EP 0 472 384 A (KOIKE YASUHIRO) 26 February 1992 (1992-02-26) column 5, line 3 - line 33; claims; figures 2,3	17,34
A	WO 93 21245 A (KABI PHARMACIA OPHTHALMICS INC) 28 October 1993 (1993-10-28) abstract; claims; examples	6-16
A	WO 95 17460 A (KABI PHARMACIA OPHTHALMICS INC) 29 June 1995 (1995-06-29) page 1, line 3 - line 10; claims; examples	6-16
A	DE 36 05 512 A (CENTRAL GLASS CO LTD) 21 August 1986 (1986-08-21) page 6, paragraph 2 -page 7, paragraph 1 page 11, last paragraph -page 12, paragraph 1; claims	1-7

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l Application No
PCT/US 99/23728

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0689067 A	27-12-1995	JP 8065251 A JP 8069024 A JP 8253758 A JP 8320422 A US 5854868 A	08-03-1996 12-03-1996 01-10-1996 03-12-1996 29-12-1998
JP 61027501 A	07-02-1986	NONE	
JP 60175009 A	09-09-1985	NONE	
EP 0472384 A	26-02-1992	JP 5241036 A	21-09-1993
WO 9321245 A	28-10-1993	AT 155501 T DE 69220950 D DE 69220950 T DK 593684 T EP 0593684 A ES 2113955 T JP 6508657 T US 5444106 A	15-08-1997 21-08-1997 04-12-1997 06-10-1997 27-04-1994 16-05-1998 29-09-1994 22-08-1995
WO 9517460 A	29-06-1995	US 5444106 A EP 0736062 A JP 9510741 T	22-08-1995 09-10-1996 28-10-1997
DE 3605512 A	21-08-1986	JP 1010019 B JP 1528893 C JP 61190546 A FR 2577565 A GB 2171706 A,B IT 1204789 B US 4617350 A	21-02-1989 15-11-1989 25-08-1986 22-08-1986 03-09-1986 10-03-1989 14-10-1986

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